

Claims

1. A method for the preparation of virus-inactivated thrombin comprising the steps of:
- 5 (a) solvent-detergent virus inactivation of a solution comprising prothrombin and factor X;
- (b) loading the product of step (a) onto an anion exchange medium;
- (c) washing the medium to remove the reagents used for
- 10 the solvent-detergent virus inactivation in step (a); and
- (d) activating the prothrombin on the medium to form thrombin by the addition of metal ions.
- 15 2. A method according to claim 1, wherein the solution comprising prothrombin and factor X is a prothrombin complex.
3. A method for the preparation of virus-inactivated thrombin comprising the steps of:
- 20 (a) solvent-detergent virus inactivation of a solution comprising factor X;
- (b) loading the product of step (a) onto an anion exchange medium;
- 25 (c) washing the medium to remove the reagents used for the solvent-detergent virus inactivation in step (a);
- (d) activating the factor X on the medium to form factor Xa by the addition of metal ions; and
- (e) loading virus-inactivated prothrombin onto the
- 30 anion exchange medium such that thrombin is generated.
4. A method according to any one of claims 1 to 3 wherein the metal ions are divalent metal ions.

5. A method according to claim 4 wherein the divalent metal ions are magnesium and/or calcium ions.
6. A method according to any one of claim 1 to 5,
5 further comprising the step of
(e) selectively eluting the thrombin from the anion exchange medium.
7. A method according to claim 6, further comprising
10 the steps of
(f) passing the product of step (e) through a filter which retains pathogens;
(g) adding a divalent metal ion and a carbohydrate to the product of step(f), and
15 (h) freeze drying and heat treating the product of step (g) to inactivate viruses.
8. A method according to any one of claims 1 to 7, wherein steps (a) and (b) are replaced by steps (a') and
20 (b'):
(a') loading a solution comprising prothrombin and factor X onto an anion exchange medium; and
(b') solvent-detergent virus inactivation of the prothrombin and factor X on the medium.
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9. Thrombin prepared according to the method of any one of claims 1 to 8.
10. Thrombin prepared according to the method of any
30 one of claims 1 to 8, for use in therapy.
11. A pharmaceutical formulation comprising thrombin prepared according to the method of any one of claims 1

to 8.

12. A pharmaceutical kit comprising thrombin prepared according to the method of any one of claims 1 to 8,
5 together with fibrinogen.

13. A kit as claimed in claim 12 wherein the fibrinogen is prepared by a method comprising the steps of:
10 (a) loading a solution comprising fibrinogen onto an immobilised metal ion affinity chromatography matrix under conditions such that the fibrinogen binds to the matrix, and
(b) selectively eluting the fibrinogen from the matrix.